

PATENT  
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Docket 091/009c

CLAIM AMENDMENTS

1. *CANCELLED*

2 to 15. *CANCELLED*

16. *(Currently amended)* A method of screening a substance, comprising:
- a) contacting a population of differentiated cells with the substance;
  - b) determining any phenotypic or metabolic change in the cell that results from contact with the substance, and
  - c) correlating the change with cellular toxicity or modulation;
- wherein the differentiated cells are obtainable by growing human embryonic stem (hES) cells on an extracellular matrix instead of feeder cells, but in a medium conditioned by fibroblast feeder cells, and then causing or permitting the hES cells to differentiate.

17 to 36. *CANCELLED*

37. *(Currently amended)* A method of screening a substance, comprising:
- a) obtaining a culture of undifferentiated pPS cells proliferating on an extracellular matrix instead of feeder cells, but in a medium conditioned by fibroblast feeder cells;
  - b) optionally causing or permitting the pPS cells to differentiate; then
  - c) combining the cells with the substance; and
  - d) determining any effect of the substance on the cells.
38. *(Previously presented)* The method of claim 37, wherein the extracellular matrix upon which the undifferentiated pPS cells are cultured is Matrigel® basement membrane matrix, laminin, or collagen.
39. *(Previously presented)* The method of claim 37, wherein the cells are undifferentiated when contacted with the substance.
40. *(Previously presented)* The method of claim 37, wherein the cells have been caused or permitted to differentiate before being contacted with the substance.
41. *(Previously presented)* The method of claim 40, wherein the cells have been caused to differentiate by a process comprising replating them onto a surface that promotes differentiation.

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42. *(Previously presented)* The method of claim 40, wherein the cells have been caused to differentiate by adding component(s) to the medium that promote differentiation towards a particular cell lineage.
43. *(Previously presented)* The method of claim 40, comprising causing the cells to differentiate into cells having characteristics of neuronal cells, glial cells, or neural precursors.
44. *(Previously presented)* The method of claim 40, comprising causing the cells to differentiate into cells having characteristics of hepatocytes.
45. *(Previously presented)* The method of claim 37, wherein the pPS cells are human embryonic stem (hES) cells.
46. *(Previously presented)* The method of claim 37, comprising determining the effect of the substance on growth of the cells.
47. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects differentiation of the cells.
48. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects expression of a marker or receptor by the cells.
49. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects release of a marker or enzyme from the cells.
50. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects DNA synthesis or repair in the cells.
51. *(Previously presented)* The method of claim 37, comprising analyzing the cells by metaphase spread.
52. *(Previously presented)* The method of claim 37, comprising determining whether the substance is toxic to the cells.
53. *(Currently amended)* A method of screening a substance for its effect on undifferentiated human embryonic stem (hES) cells, comprising:
  - a) obtaining a culture of undifferentiated pPS cells proliferating on an extracellular matrix instead of feeder cells, but in a medium conditioned by fibroblast feeder cells;

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- b) combining the undifferentiated hES cells with the substance; and
- c) determining any effect of the substance on the cells.

- 54. *(Previously presented)* The method of claim 53, comprising determining the effect of the substance on growth of the cells.
- 55. *(Previously presented)* The method of claim 53, comprising determining whether the substance affects differentiation of the cells.
- 56. *(Previously presented)* The method of claim 53, comprising determining whether the substance affects expression of a marker or receptor by the cells.
- 57. *(Previously presented)* The method of claim 53, comprising determining whether the substance is toxic to the cells.
- 58. *(Previously presented)* The method of claim 16, comprising causing the cells to differentiate into cells having characteristics of neuronal cells, glial cells, or neural precursors.
- 59. *(Previously presented)* The method of claim 16, comprising causing the cells to differentiate into cells having characteristics of hepatocytes.
- 60. *(Previously presented)* The method of claim 16, comprising determining the effect of the substance on growth of the cells.
- 61. *(Previously presented)* The method of claim 16, comprising determining whether the compound affects expression of a marker or receptor by the cells.
- 62. *(Previously presented)* The method of claim 16, comprising determining whether the compound is toxic to the cells.
- 63 to 64. **CANCELLED**
- 65. *(Previously presented)* The method of claim 37, wherein the feeder cells used to condition the medium were obtained by differentiating pPS cells.

66 to 69. **CANCELLED**

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*Upon allowance of the application, please renumber the claims as follows:*

Claim	16	→	23
	37	→	1
	38	→	2
	39	→	4
	40	→	5
	41	→	6
	42	→	7
	43	→	8
	44	→	9
	45	→	10
	46	→	11
	47	→	12
	48	→	13
	49	→	14
	50	→	15
	51	→	16
	52	→	17
	53	→	18
	54	→	19

Claim	55	→	20
	56	→	21
	57	→	22
	58	→	24
	59	→	25
	60	→	26
	61	→	27
	62	→	28
	65	→	3